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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/465,322	06/05/1995	HANS E. SODERLUND	A28203-A-FWC	1828

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EXAMINER

MYERS, CARLA J

ART UNIT PAPER NUMBER

1634

DATE MAILED: 01/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

08/465,322

Applicant(s)

SODERLUND ET AL.

Examiner

Carla Myers

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10/25/04; 10/18/04.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 97-118 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 107-116 and 118 is/are allowed.
- 6) ☒ Claim(s) 97-106 and 117 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>10-18-04; 10/25/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on October 18, 2004 has been entered.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 97-106 and 117 are rejected under 35 U.S.C. 103 as being unpatentable over Mills (U.S. Patent No. 5,221,518) in view of Dattagupta (EP 0297379; cited in the IDS of 9/8/1995).

Mills teaches methods for sequencing DNA wherein the methods require the use of the reagents of a primer, a polymerase and an admixture comprising labeled A, T, C and G deoxynucleotides and A, T, C and G chain-terminating nucleotide analogues (see, e.g., columns 26, 36 and 54-55). In the method of Mills, the nucleotide sequence to be determined is at a position immediately adjacent to or a plurality of nucleotides away from the 3' terminus of the primer (column 44). Mills teaches that the nucleotides are labeled using, for example, a radioactive or mass label. At column 44, Mills further teaches that the nucleotides can be labeled with fluorescent moieties, stating that the "The relative amounts of each base can be quantified by absorbance, fluorescence or by scintillation quantification if the nucleotides or bases are radiolabeled." It is noted that the present claims recite kits containing chain-terminating nucleotide analogues and as such the claims are considered to include chain-terminating nucleotides that are labeled with a radioactive, mass or fluorescent label.

Accordingly, the method of Mills requires the use of the reagents of a primer, wherein the primer hybridizes adjacent to or within a distance of a plurality of nucleotides to the nucleotide to be detected, a DNA or RNA polymerase (i.e., an enzymatic polymerizing reagent), and an admixture of labeled deoxynucleotides and at least two different chain-terminating nucleotide analogues. Mills does not teach packaging the reagents required to practice the sequencing method in a kit.

However, reagent kits for performing nucleic acid analysis methods were conventional in the field of molecular biology at the time the invention was made. In particular, Dattagupta (column 3) teaches packaging reagents such as primers,

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nucleotides and polymerizing enzymes in a kit. In view of the conventionality of kits and the disclosure of Dattagupta, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the primer, polymerizing agent, and an admixture of labeled dNTPs and at least two different chain-terminating nucleotide analogues in a kit for the expected benefits of convenience and cost-effectiveness for practitioners in the art wishing to perform the disclosed method of sequencing target nucleic acids.

With respect to claim 99, Mills does not specifically teach the use of primers that are 10-40 nucleotides in length. However, Dattagupta teaches that the primers used for primer extension reactions may be of a length of about 5-100 bases (columns 4-5). Dattagupta teaches that the length of the primer should be selected so as to allow for the specific annealing of the primer to the target nucleic acid under the temperature and reaction conditions in which the annealing and extension steps are performed. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used primers of a length of about 10-40 nucleotides in the method of Mills and to have packaged these primers in a kit because use of primers of about 10-40 nucleotides were conventional in the art, as taught by Dattagupta, and the use of such primers would have provided an effective means for performing the sequencing method of Mills under reaction conditions that favored the annealing and extension of 10-40mer primers.

With respect to claims 105 and 106, Mills does not teach amplifying the target nucleic acids by PCR, particularly using a primer comprising an attachment moiety.

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However, Dattagupta teaches methods for amplifying a target nucleic acid using primers comprising an attachment moiety (see, e.g., column 4). Dattagupta (column 4) teaches that the primers comprising an attachment moiety may be immobilized prior to or following PCR amplification. As taught by Dattagupta, the use of immobilizable primers provides the advantage that the amplification products can be easily separated from the reaction mixture and then used for further analysis.

In view of the teachings of Dattagupta, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Mills so as to have amplified the target nucleic acid by PCR prior to performing the sequencing reaction in order to have provided the advantage of increasing the quantity of the target nucleic acid, thereby increasing the sensitivity of the sequencing method. Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used primers containing an attachment moiety for immobilizing the primers to a solid support because this would have provided a convenient means for immobilizing the primers to a solid support prior to or following the amplification reaction and thereby would have facilitated the separation of the amplification products from the reaction mixture. Modification of the method of Mills as stated above would have resulted in a method that required the use of the reagents of a primer, wherein the sequencing primer hybridizes adjacent to or within a distance of a plurality of nucleotides to the nucleotide to be detected, a DNA or RNA polymerase (i.e., an enzymatic polymerizing reagent), an admixture of labeled dNTPs and at least two different chain-terminating nucleotide analogues, amplification primers comprising an

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attachment moiety and a solid support. In view of the conventionality of kits and the teachings of Dattagupta of packaging assay reagents in a kit, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have packaged said reagents in a kit for the benefits of convenience and cost-effectiveness for practioners wishing to perform the modified sequencing method.

With respect to claim 98, Mills does not teach sequencing primers that comprise an attachment moiety. However, as discussed above, Dattagupta teaches performing primer extension reactions using primers comprising an attachment moiety. Dattagupta (column 4) teaches that immobilizing the primers prior to or following primer extension allows for the easy separation of amplification products from the reaction mixture. Further, Mills (e.g., columns 26-27) teaches that it is desirable to separate the extension products from the reaction mixture prior to further sequence analysis. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Mills so as to have used a sequencing primer comprising an attachment moiety in order to have provided an effective and rapid means for capturing and separating the sequencing products from the reaction mixture. Further, one of ordinary skill in the art at the time the invention was made would have been motivated to have included the sequencing primer comprising an attachment moiety in the kit in order to have generated a kit that facilitated the capture and separation of the primer extension products and which thereby facilitated the method of Mills for determining the sequence of a nucleic acid.

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3. The art made of record and not relied upon is considered pertinent to applicant's disclosure.

A. Holmes et al (WO 89/09282; cited in the IDS of 9/8/95; pages 11-12) discloses methods for sequencing DNA wherein the methods require the use of an admixture that consists of dCTP, dGTP, dTTP and ddATP. During the sequencing reaction, this admixture is added to a solution containing labeled dATP. However, Holmes does not teach or suggest labeling the ddNTP in place of the dNTP. Also, Holmes does not teach an admixture containing at least two different ddNTPs.

B. Skinner (cited in the IDS of 10/18/04) teaches methods in which the misincorporation of nucleotides by AMV reverse transcriptase is studied. In one experiment (see page 6958), Skinner teaches primer extension reactions using a labeled primer together with an admix of dGTP and ddATP. However, Skinner does not teach or suggest or provide the motivation to label the ddATP in place of the primer.

C. Cohen (EP 0412883, published 2-13-91 and FR 2650840; cited in the IDS) disclose methods of sequencing a nucleic acid using an admixture of labeled ddATP, ddCTP, ddGTP and ddTTP. Cohen does not teach methods which require an admixture of both dNTPs and ddNTPs.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach

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the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571)-272-0745.

The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866)-217-9197 (toll-free).

Carla Myers
January 19, 2005


CARLA J. MYERS
PRIMARY EXAMINER